# The Morton Lecture

ON

# CANCER AND CANCEROUS DISEASES

DELIVERED AT THE

## Royal College of Surgeons of England

*on Monday, the 18th November, 1889*

BY

JOHN MARSHALL, F.R.S., F.R.C.S.

LL.D. Edinburgh, M.Ch. (Hon.) Royal Univ. Ireland

PRESIDENT OF THE GENERAL MEDICAL COUNCIL

EX-PRESIDENT OF THE ROYAL COLLEGE OF SURGEONS OF ENGLAND

EMERITUS PROFESSOR OF SURGERY, UNIVERSITY COLLEGE, LONDON

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TO MR. J. T. MORTON

TO THE PRESIDENT, VICE-PRESIDENTS, AND COUNCIL

AND TO THE FELLOWS AND MEMBERS
OF
THE ROYAL COLLEGE OF SURGEONS OF ENGLAND

THIS LECTURE IS DEDICATED

BY THE AUTHOR

# The 'Morton' Lecture

ON

# CANCER AND CANCEROUS DISEASES

Mr. President and Gentlemen,—I am of course reminded in this Institution that I am within a very short distance of a splendid Museum, from which I could have drawn a superabundance of material to illustrate the subject of this lecture; but my own impression is that it is far better for a lecturer, on a special occasion like this, to provide himself with his own material, and rely upon that or on materials given to him by his friends, rather than to enter, as it were, into the domain of our vast collection, and perhaps overburden himself with its superabundant material. I have therefore selected a certain number of objects which have been supplied to me by my friend Mr. Robert Boyce, Assistant in the Pathological Department of University College; and through his ability and earnest work I hope to have an opportunity of allowing you to see certain specimens under the microscope, and certain pictorial representations on the screen, which will illustrate certain portions of the subject which I have to bring to your attention.

By the rather illogical term 'Cancer and Cancerous diseases,' I presume it is intended that one should consider not only so-called true cancers, but sarcomatous tumours, and those which contain the elements of both—mixed tumours,—and not to travel beyond that line. On the present occasion, however, I must limit myself almost exclusively to the true cancers, for the subject is so vast that it is quite impossible to

overtake every branch of it in one lecture; and if I were to attempt more I should most signally fail.

The term 'true cancer' should be, I think, associated with those growths that depend primarily upon an over-development of a spurious form of *epithelial*, or *mesothelial*, or *hypothelial* tissue. I use the word *mesothelial* because it seems convenient to have a term to distinguish those distinct forms of epithelioma which originate in the middle layer from those which commence in the upper layer or in the under layer of the embryo. I shall therefore speak occasionally perhaps of the epitheliomata, the hypotheliomata, and the mesotheliomata. We are apt also often to speak of these growths as being more or less *embryonic*, and the term is an exceedingly happy one —very good indeed—because it implies the incompleteness, at any rate, of the tissues of which these tumours are composed. At the same time, if used in too sharp a sense, it is untrue, because I contend there is nothing in the embryo like what you find in cancer, nor is there any cancerous element in the embryo itself. There is, in fact, a strange divergence from the embryonic forms in these epitheliomatous and hypotheliomatous tissues—a strange divergence, which I would rather characterise by the word *anarchy*. They are *anarchical* evolutions from the embryo or from the embryonic tissues; and this is a very important matter, because we are apt to suppose that an inference may be built upon that word embryo or embryonic—namely, that the elements of these tissues may originate in a process of reversion to a true embryonic form. Now, if they were distinctly and absolutely like embryonic tissues, I should admit that theory; but until I find in a cancerous growth a distinct reproduction of the pure embryonic elements, I say that it is a dangerous expression, very likely indeed to shut up inquiry, to limit our investigations, and to induce us to pass glibly on, satisfied with the explanation that these are embryonic tissues. They are not embryonic tissues; they are like embryonic tissues; they originate from them even as the whole body does; they are part of the body, but they are not distinctly embryonic tissues; they are, as it were, irregular, uncontrolled tissues, and I would speak of them specially as *anarchical*. I would speak of them as *anarchi-*

*morphic*, *anarchi-bolic*, and *anarchi-synthetic*—as building up a texture.

Clearing our way, then, we pass on to consider what is the character and what are the surroundings of these tumours. And here I of course throw myself upon your own experience; for it must be just as great as mine in regard to the painful history of these perilous growths as a general process. You know how they begin, how they progress, and you know their termination as well as I do. Nor do I dwell upon the particular conditions, significations, or qualifications of this or that stage of their development; and if I do not trouble you with remarks on the influence of age or of sex, of hereditary tendency, or of occupation, or of diet, it is because I assume that you know about these points as much as I do.

I pass therefore directly, as far as I can, to inquire what is the *cause* of cancer. And no doubt everyone here will say, 'We know not the cause:' and in that I entirely agree. But does this prevent us from endeavouring to ascertain the cause? Are we not compelled as members of a scientific profession to dive into this mystery? Is it likely that Providence has, as it were, struck such a fatal and fearful blow at the human construction, that there is no remedy for our ignorance, no knowledge but that which we now possess? We most surely stand in a position between the past and the future; and we are responsible for carrying on this investigation and inquiring into this disease until we know something more about it. Therefore there needs no apology for attempting the solution of what now seems to be an insoluble problem.

But let us see how it has been approached in past times, and let us be encouraged, if we can, by ascertaining the mode in which and through which knowledge has been advanced in regard to these important diseases. And here I claim that the most advance has been made through the study of *structure*. We, of course, know the importance of studying the pathological relationships, the history, the development, and the surroundings which are worked up, as it were, in this intricate problem,—those also of nation, of race, of family, of hereditary influence, and so on; but we cannot conceal from our minds, I think, that, being a structural condition

affecting the living economy, it must be through the structural element that we must first try to reach the truth. Such has been the case; for if you study the *older* descriptions of this disease you will see that they are especially remarkable for the keen appreciation of their conditions of growth, their whereabouts, the progress they make, the general career, as it were, of these tumours; but the Writers were specially ill-informed as regards their structure. If we take a most admirable Thesis by one George Tabor, published upwards of a hundred years ago in Haller's splendid 'Disputationes Chirurgicæ,' we shall find that he gives a most characteristic account of a cancer of the breast. He speaks of the *epidermis* by name, of the soft tissue, of its extreme vascularity, of the union of the ducts with the acini of the glands; and then he adds that there are two sets of lymphatics—which of course we now know to be an error—one conveying material to the breast and the other bringing it back. Then he proceeds to speak of the life history of the disease, and he characterises the whole in a few remarkably vivid touches, expressed in a Latinity which we seem to have forgotten, embodying in a few sentences, or sometimes in a few words, what we now spread out into a paragraph.

Now, how have we advanced since that time? Plainly by *anatomical* investigations in the first instance; and if I venture to put upon the screen an illustration of what has been done in the past, and then come to what we know in the present, you will see that our advance since Tabor's time has been most remarkable. The diagram before me represents the plate in Dr. Walshe's 'Cancer,' which was executed on steel from drawings by myself in the year 1846. You will find in this illustration that we knew then something more than our friend Tabor. In the centre you will see the section of a cancer of the breast. It is hard, scirrhous, with fatty lobules round about, and with many of the marginal glandular acini still unaffected. You will see that we were able at that date to illustrate its peculiarities of structure, and to associate these by comparison with natural elements in the body: the red blood-corpuscle, the white blood-corpuscle, the healthy epithelial particles, then unhealthy epithelial cells, more marked

on this side, and still more wild-fashioned epithelial elements, and yet more wild-looking growths in the heart of the cancer. Here you also see the remarkable *stroma* to which I shall have to direct your attention by-and-by—the peculiar stroma that surrounds the acini which contain the *so-called* cancer *cells*. I bring forward this plate merely to show that in the hundred and thirty years that intervened between Tabor and Dr. Walshe, the advance in knowledge was not in the history of the disease, not in its development, not in the peculiarities relating to sex, and so forth; but was in the extent of our knowledge in reference to its structure. I maintain that, in dealing with this point, I afford the key to the most material advances which have yet been made in regard to the nature of this disease. So that, I think, anatomy must still be the first path of inquiry.

I will now show some specimens to illustrate by example the mode in which anatomical research has already given us much more knowledge than we possessed in 1846. First of all, in regard to the *so-called cells*, I am afraid it is too frequently the case that in using the words epithelial and epithelioid cells, we have neglected or ignored the particular deviations which these cancer-cells certainly manifest, when you compare them with healthy epi-, meso-, or hypo-thelial elements present in the embryo. In the embryo all is methodical; all the cells of these tissues are undergoing a straightforward and well-defined career, not pressing each other out, not squeezing for victory, not forcing against any other tissue, but each co-ordinated to its destined end, and marked in the most peculiar way by characters leading to that end. Now, if you examine the epithelioid element in cancer you find distinct divarication, and divergence from all that. What does it amount to? You are familiar enough with the forms of these cells, so that I need not sketch them; but you will allow me to remind you that the important part of the cell, according to modern physiological notions, is the so-called *nucleus*. Now, the nucleus governs, as far as we can understand it, the development, the evolution of the cell, as well as its multiplication. What are the peculiarities of the nucleus in a cancerous cell? They are usually described in a very

perfunctory manner. But have we not new methods of analysis? Have we not methods of investigation which will penetrate a little deeper? I fail to see, until recently in a paper by Dr. Heneage Gibbes, that there have been any effective researches into the *modus operandi*, as it were, of the nucleus of a cancer cell. He has undertaken this inquiry, and Dr. Lauder Brunton is following on the same lines in using various tests of colouring agents for the purpose of discriminating between different layers or strata of healthy cells, in this way following Dr. Gibbes, in his attempted discrimination of the different changes recognisable in the cancer cell. These reagents will help to unfold the mystery which is lodged in the nucleus. We know that the nucleus has important properties originating from the combination of seminal and germinal influence, developing the whole body, developing even the cancer which grows within the body. Now this germinal and seminal development has been shown to be associated with remarkable movements and changes of form in the core of this little bit of a nucleus,—most wonderfully tufted columnar arrangements, feathering themselves out this way and that; and it is through the agency, no doubt, of this internal economy, through these remarkable changes, that the healthy embryonic cell, the germ-and-sperm cell, gives rise to the later embryonic cells which carry on the development still further. We must endeavour to search out this mystery, to look into the minute anatomy and work of the nucleus of the cancer cell. That is a hopeful, and it does not seem to me at all an impossible, thing. We shall find it, no doubt, *anarchic*, but may we not be able to trace the steps of the anarchy? Shall we not hope, as it were, to unfold the mystery of mysteries which lies in the nucleus of a cancer cell?

But if we proceed further with regard to these cells, we find it is not only their *structure* which we must study, but we must study their *composition*. And here, again, it is by the agency of different tests acting upon them that we are able to discriminate between certain important portions of a healthy cell. Why should not this mode of analysis be applied, at once, to an unhealthy cell? Are there not swarms of agents

in nature—colouring matters, chemical substances, and other things—which should be forthwith tried, to see whether we can develop by this sort of polarisation—not of light, but of chemical agency—abundant characters in these unhealthy cells which will lead us to see how they become *anarchic* and unhealthy? Then we must apply, of course, to the chemist, because these cells are not only anarchic in their form and evolution, but in the products which they yield. They are not only *anarchi-morphic*, but *anarchi-bolic*. The healthy epithelial cells stand out amongst the secreting agents of the body. Their function is not merely to cover up and protect, but they have functions beyond that—metabolic functions of separating from the blood secretions of an infinitely varied kind, and that must be done through mechanism and chemical affinity. It is no use supposing that the process is blank. It is no use believing that a salivary gland cell is the same thing as a mammary gland cell; that cannot be. There must be some hidden secrets in the very substance, as in the very mechanism, of these cells, which give origin to their metabolic action. There must be not only a peculiarity of structure as between the different glands in these little cells, but that must be associated with peculiarities of substance. And here we want the chemist to come in; we want chemical investigation of the highest character, and we are approaching the time when we may hope that chemists will take up these points. We have them already engaged in investigating the poisonous substances which occur in the dead body from decomposition, and other poisonous products which occur in the living body, such as the leucomaines, automaines, and toxines, things that may develop sometimes by foreign agency, as we know, and sometimes in a spontaneous manner; and we call upon chemists and demand their assistance, and we urge this on the younger members of our own profession who are showing zeal in various ways at home and abroad. We must take care of our honours, for foreigners are close upon our heels, and are even surpassing us; we must urge on our young chemists to take up these matters; and very soon opportunities will be afforded them by the Conjoined Colleges to undertake inquiries of this kind. It would, I say, be a

pity—I dare hardly call it a shame—if some did not come forward and push on investigation in regard to these serious and calamitous forms of disease.

Now we see that metabolism, as well as the mere mechanical thrusting in of these morbid elements into the body, must be seriously at work, and we ask that that metabolism should be investigated. The epithelial cells are essentially secreting or excreting structures; although deformed, although disordered in their arrangement in cancers, that part of their duty is going on, but not going on right; it is going on wrong. What do they produce? Very many years ago I took a cancer immediately after it had been removed by Liston in the theatre of University College Hospital, and within a minute I tested the juice of the cancer, and found it acid. By degrees I found that this observation was not unique, and in fact it had been repeated and asserted over and over again, so that I thought little of it at the time; but it leads one's mind back at this moment to the thin edge of an inquiry—what is the acid? I tried to find it out, but with the imperfect means at my disposal, and my imperfect knowledge, I could not say anything more than that it yielded an acid and viscous liquid when it was evaporated, and I thought it was lactic acid. But I do not believe that lactic acid, by itself, is a sufficient answer to this inquiry. Here, therefore, looking at the secreting power of these cells, I say we ought to investigate, and we ought to have investigated, what it is that they secrete or excrete.

Such chemical researches will be most material for the subsequent examination of what takes place with regard to these cells. I have designated their behaviour as anarchical. Now, what is the great governor of the body? The nervous system. It is very well to say that tumours can be developed in vegetables as well as in animals. Are we sure that this analogy is true? The world is full of analogies. A man in a certain sense is like a carrot, but he is very different; and so these cellular over-growths in plants, caused by irritation or puncture, must lead us to study in a most interesting way the possible alliance or analogies between them. But that must not mislead us; we must not suppose necessarily that

an anarchical growth in a plant is quite the same thing as an anarchical growth in an animal. The anarchical growth in a plant may, however, be due to a disturbance or complete detachment of that little protoplastic fibre which has been shown to run through many vegetable cells from cell to cell. With the growing plant there is a fine, delicate protoplasmic fibre, which has been long overlooked, indeed only quite recently detected, which seems to govern the evolution of the outgrowing cells of the plant. Now, is there no such thing as that in the animal cells? Is there no connection between the governing fibre—which really lays down, as it were, the rule of form and structure—and the complications of the structure of the human body or the animal body? It may be said that there is merely an adaptation of the form of a given nervous system to the form of a particular animal. I disbelieve that altogether. I believe strongly and firmly that the nervous system is the centre which lays down and commands the growth of the body in this, that, or the other direction. If not, what does it do? I can understand that in the centre of the foundation cell there should be a molecular movement which will give onset, as it were, and impulse to the growth of that cell. I can suppose that; but when once that cell has multiplied itself into hundreds and thousands, can I believe that that cell, or its actual contents *per se*, still govern the body? No, the contents of that cell, the products of this nucleus, must be growing all the time in the other cells, and must shoot out into them and command them to go thus far and no farther, and to develop in this way and not in another. At all events I believe this may be, although you may regard it as too hypothetical.

But let us now ask what happens with regard to cancer. Has anyone ever shown, as distinctly as has been shown with regard to the secreting cells, that the epidermoid or epithelioid cells of cancer are under the influence of the nervous system?

Not many years ago we were very much struck with the fact then expounded to us that distinct nervous filaments had been traced into the corpuscles of the salivary gland. I saw drawings of these, yet I would hardly believe it. I thought

it too wonderful to be believed, but I gradually became accustomed to it; and now we know that nerve filaments do penetrate into normal epithelial tissues. I may mention a case that occurred to myself only this last year, that of an extremely sensitive tumour which I removed from the lip, and which, on investigation, my friend Mr. Boyce showed me was teeming—although it was a thick piece of epithelium, having many layers where there plainly ought to be only a few, accumulated layers of epithelial cells growing from the rounded to the oval, and from the oval to the flattened form—with these little nerve filaments, exquisitely minute, running up between the rounded cells to reach the oval cells and others, and finally becoming lost, because the epithelium had done its work, and was about to be cast off. We know it has been demonstrated that a nerve, a commanding thread, an electric cord, as it were, passes into each individual cell; and what can be assigned as a function to it except that it is the governing cord, the co-ordinating fibre of its life? The blood nourishes the cell; the lymph carries away its wasted or unused material; a duct conveys away its secretion. But what does this nerve fibre do? It gives sensitiveness, no doubt, in its own cell way, of the presence of external stimuli, not necessarily a consciousness of sensation. With a cut nerve there may no longer be any such sensitiveness, but the cell is not destroyed. In the salivary gland the part from which the nerve is divided may go on secreting; so may any other gland *for a time*, so long as the cells are in function and in health; they dwindle by degrees, but for a time may go on secreting. But the final control of the health and of the life of a cell must, I contend, be in the nerve filament; for I do not see in what other way it can be materially governed. In science we may not assume extra-material agencies. We may try to conceive whatever there may be behind—that is, the great unknown—but we are bound in this world to follow out material actions and changes, and not to be satisfied until we have traced every function through structure. With such function, or behind that, comes life, the original endowment which we can never understand and hardly conceive; but once life has been imparted, it goes on in structure; and

we may find out in structure everything which results from its evolution and disturbance.

Has anyone examined from this point of view the epithelioid cells of cancer? I have myself, and I cannot believe that when they are aggregated into these irregular masses and groups, when they penetrate along the lymphatic spaces as they do through the body, when they reach the lymphatic glands far away from any primitive nerve fibre which could possibly have once reached them, when they advance into distant tissues, when they recur in a cicatrix—I cannot admit, without actual demonstration, that the nerve fibres go on with them, so as to regulate their disordered and anarchic government. We want to know this; and here is work for the microscopist, to study carefully in an early yet well-developed growth, in a recurrent growth, in a lymphatic or a lymphatic gland, the connections of possible nerve fibres with the epithelioid cells. We want an answer to that. I feel strongly upon this point. I suspect what the answer will be, from my own rude investigations. I can hardly suppose that in the pell-mell agglomeration which we see in a cancer, each cell has its own proper guiding nerve fibre. But how and why may we suppose that these nerve fibres are severed? It may be simply from the extreme rapidity of the cell-growth; and this may afford one indication of the mode in which cancer originates from a comparatively healthy tissue. In the healthy formation of epithelial tissue, the nerve tissue would still remain in it; but in the overgrowth excited by some long-continued or specific injury, the cells at last break away from the nerves; they retain the power of multiplication within themselves, because each cell, like the cell of a minute infusoria creature, contains the quantity and kind of material which is necessary to build it up, but it does not retain the continuous governing tissue with its power of control, which must be retained by a centralised nervous system; and as soon as you pass from the unicellular animal to animals composed of many cells, you find the governing power, the control, in the presence of a nervous system. Now, why not try to solve this problem? It seems to me to lie at the root of a great deal of the explanation of cancerous growth. Even if it be shown that the

primitive stimulus, the primitive irritant, is not a common irritant but a specific one, even if it be a bacillus or a bacterium, or any of those minute bodies which are supposed by some to be responsible for cancerous growths, even then the severance of the cell from its nervous connections may lie at the root of the explanation of this anarchical form of growth. Of course I put it as a theory, as my own impression; I do not think it is established. I should be sorry for anyone to say that I adopt it in that sense; but I do think there is a great deal in it, and that, unless we can ascertain whether the nervous filaments do enter the cells or not, we are ignorant of a fact which we ought to know. Not only the growth of the nuclei, the characters of the nuclei, the mode in which they develop the cell itself, but the mode in which the cells are connected, so as not to be anarchical, should be made a matter of immediate and profound investigation—to say nothing of any influencing changes occurring in the great nervous centres themselves.

We come next to the further question, What are the products of these cells? I mentioned that they were acid, but that is a very poor result. We must know more about them, in what tendency they run, what are their secondary products, and what will be the action of those products upon surrounding tissues. They may be the very agents which destroy the nervous connections; they may, at all events, be the very products which alter the stroma around and help to dissolve materials, and carry them into the lymphatic spaces and channels so as to cause a dissemination of the disease. It is not necessary that a very large particulate cell should pass into a lymphatic channel in order to spread this disease; a very minute nuclear particle might suffice; or again such particle might not be a particle of the cell itself, but a foreign product, though my own view is that it would be a particle of the cell itself.

Now let us proceed to the question of the *stroma*. The stroma of cancer is acknowledged to be one great peculiarity of it, as distinguished from the basis of an ordinary sarcomatous tumour, distinguishing it from sarcoma as much as the sarcoma cell itself is distinguished from the epithelioid cells. This stroma of cancer is a very remarkable substance. Long

ago, in my Class lectures, I defined it as a spinous-looking structure. When you have washed away the cells and disclosed the little loculi of the cancer, you find a crisp, fibrous, sharp, clear, bright-looking tissue, absolutely different from the areolar tissue of a simple tumour or from healthy fibro-areolar tissue, yet no doubt developed from it. Its bands are hard, glistening, vitreous-looking, and break off short; it does not run in the beautiful undulating lines of areolar tissue, but encompasses the cell-masses with curved bands of a most peculiar kind. It is always developed *pari passu* with the quantity of cells, provided the tissue in which these cells are developed is a firm tissue—the tissue of a firm organ. It is harder in the mammary gland than in the salivary gland; it is harder in the salivary gland than in the liver; it is softer still in the lymphatic glands. Of course, the lymphatic gland has a web-like basis which is capable of this remarkable transformation. I say that this stroma has not been sufficiently studied. I do not think we know enough about it. Its curious, hard, shining, glassy character is further associated with that peculiar crispness when cut, that creaking sensation which, in certain advanced stages, becomes almost bony to the scalpel edge; it resembles in a remarkable way, not as a highly organised and regular tissue, but in certain characteristics, the periosteal fibres of a growing bone which is developed from membrane, not from the cartilaginous basis of the bone. In Quain's 'Anatomy' you will see something which will remind you of the spinous character of this cancer stroma, of which I hope to be able to show you some representations on the screen. I do not say that the growing bone fibres are like the stroma of cancer, but the stroma of cancer shows a sort of likeness in that direction.

And this leads me to say that chemistry will herein aid us, because long ago it was pointed out that cretification is one of the conditions apt to follow upon the atrophy of cancer, especially in the breast; and the cretification or hardness of the stroma is accompanied by a deposit of lime salts in the little loculi themselves. So that here we find hardness and crispness and a likening to periosteal growth, associated with the presence of lime. Many years ago I had a special analysis

made for me of this peculiar tissue, and the result was that its ash contained three or four times the quantity of phosphates that the ash of a healthy piece of mammary gland did. There was nothing remarkable in that, because the fact had been demonstrated by the microscope, and represented by Dr. Hughes Bennett many years ago, in beautiful illustrations of this interpenetration of tissue by a kind of calcified substance. Now this is extremely interesting, because it raises the question, What is the function of the stroma, and what is its origin? Is the stroma a part of the cancer? Is it part of that extraordinarily powerful disease which invades the body and which produces these tumours in the healthy tissue, or is it not? Now, it seems to me there are two very widely different opinions here, but there is one which is more commonly expressed than the other. It has been held by most writers that the stroma is a mere web that holds the cancer cells; that it is produced by the irritation of those cells; and that by degrees it may consolidate itself into such a hard, firm form as to crush the very cells under the influence and agency of which it has been developed. This, of course, leads the mind at once to a possible mode of killing these forms of disease; we cannot say that it will lead to that, but of course that is an inference easily and naturally drawn from it. But what I want to see is to have this stroma investigated; I want the anatomist to pay a little more attention to it, to show in what it consists. It is utterly unlike the wavy forms of the filamentous tissue; it seems to be more as if such bands were crushed up together, moulded as it were together, pressed into an indifferent form (if I may use the word), and then impregnated with earthy salts in some peculiar way. Now the acid secretion of the cells, finding its equivalent in earthy matter, may penetrate this peculiar tissue, and may give it its character; and surely we may learn something more of it if we know its chemical constitution and its relation to the surrounding areolar tissue.

I shall now be able to show you, I hope, some of the progressive changes which take place in the areolar tissue towards the formation of this peculiar stroma. Here is a compressed mass of cancer cells with stroma passing through

it. You see this peculiar structure with its compressed nuclei branching through it. You see how extraordinarily different it is from the ordinary areolar tissue. I think myself that the history of this stroma has been neglected. I think that we may learn a great deal by a more patient and thorough investigation of its structure, mode of formation, and chemical composition. Through such researches, through a more minute study of the cell growth itself, and its organic and chemical relations, and a more deep and profound study of the stroma, I think there are many problems which will in time be answered; and I trust that those answers will contribute to lighten our task in combating this painful disease.

Reserving till after the lecture the demonstration of the remaining figures, I must omit what I hoped to say about the *blood* and *lymph*, and add a word or two about the mode in which this cancer *invades* the surrounding tissues. If the cancer cells secrete certain products in superabundance—and that they have secreting powers is certain, for that is their primitive epithelial function—if they secrete something which induces the formation of the stroma, this agent may also serve to dissever the *materials* of the cells themselves, and help to carry them on into the lymphatic spaces as they are called, and so into the lymphatics, and onward to distant parts. But the stroma fibres may also break down the limits between the epithelioid formation and the surrounding tissue; they may be the carriers along which the disease spreads; and therefore, I say, the more we know of their nature, the more we may hope to arrive at a time when possibly, by remedies, we may stop the growth of both cell and stroma, stop the production of these unwholesome products, and stop the invasion into the surrounding tissues, and perhaps—if it can be shown that that is a right procedure—may harden the stroma and thus crush the cells in their nests. The invasion of cancer must come about, I assume, in this way. The elements must pass into the intervals between the surrounding tissue; they must get into the lymphatics, and so must reach the lymphatic glands. The proof of this is that the lymphatic glands in the neighbourhood are always the first to be infected,

and there it is again we ought to study the remarkable and specific constituents of cancer growth.

As to the *recurrence* of cancer—I do not mean the spread of cancer through the system, or by the agency of lymphatic glands, and so into the blood—but I speak of local recurrence after the removal of the cancer; this also affords us a most advantageous field for investigating the isolated properties of the cell and stroma.

In recurrent growths the cells abound; in recurrent growths the stroma is scanty; in recurrent growths, therefore, we should find the anatomy and physiology, so to speak, or the pathology, of the cells much more easily followed than in the primary growths. There cannot be a doubt that most frequently this recurrence takes place; and there is one important practical point which I wish to impress upon you if I can—that the true recurrence which takes place locally and on the margin of the site of old disease begins in atoms of diseased tissue which have been left behind. It is possible for an operator to say, 'I know I have completely removed this tumour, and it is utterly impossible anything can remain behind.' But when you consider the number of lymphatic spaces, the smallness of the diseased units, and the facility with which these will creep through the healthy tissues, and the impossibility of detecting with the hand or eye how far they have gone, you will see that it seems much more probable that the recurrence should be due to a local extension of the primitive disease rather than that it should be a new growth altogether. If it comes in a lymphatic gland, if it comes along the path of lymphatics, that is obvious; but we speak of recurrences near the growth, and those recurrences I have lately been studying, and I quite agree with Heidenhain that they are on the margins of the old incisions. In this enlarged photograph of an early recurrence, a very small one, you will find that the growth is not in the cicatrix; the cicatrix is composed of dense fibroid tissue like an ordinary cicatrix; but exactly in the margin between that and the healthy tissue there is found a growth springing up. It may invade the cicatrix, but it goes a long way into the surrounding tissue first; and I have never found one in which I have seen it

actually come *in* the cicatrix, but always at the margin, or, what is sometimes very deceptive, directly *beneath* the scar, which it may then invade. But suppose it did come in the cicatrix, what is the cicatrix? The cicatrix is a product of the body; it is a modified form of areolar tissue produced after accident, and intended not to kill but to heal, to repair; and therefore it is a part of the frame, and most surely contains its little channels and paths through which a morbid growth may extend. It is possible, therefore, that from the margin of the pre-existing tissue the cicatrix may itself become early involved; but it happens here that the small recurrent nodule is not in the cicatrix, but in a thickened part of the surrounding tissue loaded with stroma. Now here, again, the lesson that we learn is a perfectly obvious one, one which I myself have learnt a long time ago; and that is to disregard the neatness of an operation, the closeness of incisions to the tumour, but to sweep far away beyond what you really estimate may be the seat of the disease. Do not be timorous and hesitating; do not care about a scar, but sweep away to a great distance; follow the tissues up especially towards the axilla, especially when the tumour is on the axillary side of the mammary gland. Remember also that there are deep-seated tumours in the mammary gland, and that these usually have their lymphatics going not to the axilla, but through the intercostal spaces and directly into the thorax, or through the pectoral muscle, along under that, and so reaching cervical or thoracic glands beyond. The position, therefore, of the growth in the mammary gland is of extreme importance. If it be central, you do not know where it may extend and affect the lymphatics; if it be to the outer side, which is more commonly the case than in any other position, it is nearly sure to affect the axillary glands; if it be deep seated, it may pass into the intercostal spaces through the pectoral muscle, even long before there is any mischief in a lymphatic gland within the thorax, or in the axilla, or the neck. The spaces between the muscular fibres and the spaces under the muscular fibres may be involved; this I have seen over and over again in a most characteristic way. Mr. Boyce has come here to my assistance, and gives photographic demonstration of the fact that the

cancer cells do really impregnate, as it were, the deep-seated muscular tissue and the spaces between the muscular fibres, and unless these are removed a return is almost sure to occur. The old form of sweeping operation therefore should be always held in respect. I believe that its good results, which were perfectly astonishing, depended on that. It does not matter about deformity—it is the preservation of the patient's life; and a very sweeping use of the knife is better, I would say, than any cautery, any yet tried electricity, any form of temporising with caustics, with pressure, with cold, or any such means. They may answer, and in future that great force of electricity, now again on its trial in a special form by Dr. Inglis Parsons, may come to be specially useful. I admit its value, and wish it all success; but at the same time remember that it will only destroy what it reaches, and although it is extremely remarkable to find that the cancer tissues seem to dwindle under its influence whilst the healthy tissues resist it, still, remembering the acid juice of cancer, remembering the mode in which it penetrates into the vacuities of the living tissues, what a tendency it has towards them, and remembering that in spite of electrical destruction this may go on, and then considering, again, the requisite repeated application of electricity, which comes to be like the repeated application of a cautery of a simple character—remembering all this, I say we may find that it will ultimately be regarded as inferior to the knife.

The knife, which sounds so cruel, but which is not indeed cruel under the influence of anæsthetics and the use of antiseptic treatment—the knife is the most feasible method of removing these growths. After the knife, however, I certainly in my own practice, where I have the slightest doubt as to the complete extirpation of the growth, apply some kind of acid caustic. I do that, and I have found it extremely valuable.

I have not cumbered this lecture with personal records of cases, but when I look back to my whole experience I find some very successful ones in which accidental hæmorrhage came on, and in which I had to undo a wound and apply powerful caustics—perchloride of iron, and perhaps chloride of zinc. There are special cases which I could point to in

persons living and now perfectly well, eight, nine, ten, eleven, and twelve years since operations of that kind. Comparing these cases with the hesitating use of the knife which formerly I myself practised, keeping as near to the growth as I was told to do by my teachers, as near to the tumour as possible without of course leaving any ostensible mass behind, still keeping close to it—when I compare these later cases with those I had under observation twenty or thirty years ago, I say their success is very remarkable.

It is truly gratifying to find that more permanent benefit follows in proportion as you remove tissues, in proportion as you work up to the axilla and remove the axillary glands, and even cauterise the floor of the wound if there is the slightest sort of suspicion about that part. The gratification which one feels at the success of these operations compels me to insist on this as a most important practical point, and a lesson never to be lost sight of.

Now, Mr. President and Gentlemen, the hour is about to close. Of course you all understand that a lecture of this kind is but playing on the surface of a great subject. If it is ever published, I may venture to append or introduce here and there illustrations that will carry, perhaps, conviction to some of your minds who may not quite have followed me in all I have said. But in the meantime I thank you for listening to me for this hour, and I invite your attention to the diagrams and to the preparations which are upon the table.

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Note.—In publishing this Lecture separately, as revised from a verbatim shorthand report, I gladly repeat what I have already stated elsewhere, that I fully recognise the prior claim of Dr. Inglis Parsons, as regards the originality and publication of similar suggestions to my own, with regard to the emancipation of cancerous growths from the influence of the nervous system. At the same time, I reaffirm my earlier and completely independent arrival at those suggestions.

It has since transpired that Sir Peter Eade, of Norwich, had many years ago published similar views.

But, as distinctly stated in my Lecture, it is by no means

established that these suppositions are correct. Indeed, the whole subject of the relations of the nervous system to ' new growths ' of all kinds, whether simple or malignant, requires to be carefully inquired into. This is one of the several paths of research which it was the main purpose of my Lecture to urge upon the attention of the rising Pathologists of our day. For myself, I always taught in my classes that although nerves were found attached to or embedded in cancerous or other tumours, there was no evidence that they were distributed to or belonged to the tumour-tissue itself.

I propose immediately to prepare and publish some further considerations and suggestions on the subject of ' Cancer,' in the form of an Appendix to a re-issue of this Lecture.

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SPOTTISWOODE AND CO., NEW-STREET SQUARE
LONDON